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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/053,291	01/17/2002	Heidi Stuhlmann	A31200-A - 070165.0467	7117

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EXAMINER	
WILSON, MICHAEL C	

ART UNIT	PAPER NUMBER
1632	

DATE MAILED: 12/09/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/053,291	STUHLMANN ET AL.	
	Examiner	Art Unit	
	Michael C. Wilson	1632	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *28 October 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-6* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-6* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Applicant's arguments filed 10-28-04 have been fully considered but they are not persuasive.

Claims 1-6 remain pending and under consideration.

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Oath/Declaration

A copy of the original oath/declaration filed in parent application 09/083290 was filed with the instant application.

Specification

The preliminary amendment filed 1-17-02, has been entered. Applicants amended the paragraph beginning on pg 14, line 16, by filling in the blanks with a date and ATCC Accession Nos. on page 15. Proof of deposit provided by applicants indicates Plasmids mVezf1.1, mVezf1.2 and mVezf1.N were designated ATCC Accession Nos: 209873, 209874 and 209875, respectively, on May 19, 1998.

Claim Rejections - 35 USC § 101

Claims 1-6 remain rejected under 35 U.S.C. 101 because the claimed invention lacks patentable utility. The specification states the DB1 gene is expressed in human blood cells and adult organs, but the function of the DB1 protein is unknown (pg 6, ¶ 3, of the present specification). The specification states the Vezf1 gene is 98%

homologous with the DB1 gene and is expressed during vasculogenesis and angiogenesis (pg 41 and 42). The specification does not provide a function for the Vezf1 or DB1 proteins. It is not clear that the homology between Vezf1 and DB1 is sufficient to give the protein products the same activity. The specification does not compare the homologies of Vezf1 or DB1 proteins with any protein with a known function such that the function of Vezf1 or DB1 could be determined with any certainty. While the DNA claimed in the instant invention may be used to make protein or to test for gene expression, such a use is not of value if the function of the protein is unknown. Without a readily apparent utility for the protein, it is unclear that the purified and isolated Vezf1 gene (claim 1), the purified and isolated nucleic acid encoding the Vezf1 protein (claim 3) or the expression vector containing the DB1 gene (claim 6) have any utility. The Vezf1 gene and the DB1 gene do not have a known function in the instant invention and consequently do not have a readily apparent utility.

Applicants argue the specification asserts using the Vezf1 gene as an endothelial cell marker on pg 7, lines 11-13. Applicants cite Xiong (Dev. Biol. 1999, Vol. 206, pg 123-141), which states Vezf1/DB1 was restricted to endothelial cells and their precursors and point to Fig. 9-12, pg 41, line 8, to pg 43, line 11. Applicants' arguments are not persuasive. Xiong taught Vezf1 was restricted to vascular endothelial cells and their precursors (1st line of abstract). Pg 7, lines 11-13, state the "invention provides for a method of identifying an endothelial cell, comprising identifying the expression of a Vezf1-encoding RNA or Vezf1 protein in the cell." The specification does not state Vezf1 is restricted to endothelial cells. In addition, the specification is generic and

states Vezf1 can be used to identify any endothelial cell, while Xiong taught Vezf1 was restricted to vascular endothelial cells. Since Xiong was not available at the time of filing, and the teachings in the specification do not teach using Vezf1 was specific to vascular endothelial cells, it is not readily apparent that applicants knew Vezf1 was specific to vascular endothelial cells at the time of filing. It is not readily apparent from Fig. 9-12, pg 41, line 8, to pg 43, line 11, that Vezf1 was specific to vascular endothelial cells. Without such guidance, the asserted utility on pg 7, lines 11-13, is not specific because it is not specific to vascular endothelial cells and does not state expression occurs only in (vascular) endothelial cells.

Applicants cite Aitsebaomo (J. Biol. Chem. 2001, Vol. 276, pg 39197-39205), which states Vezf1 is an endothelial cell-specific transcription factor that regulates expression of the endothelin-1 promoter. The specification does not teach function of Vezf1, i.e. regulating expression of the endothelin-1 promoter as described by Aitsebaomo. Since Aitsebaomo was not available at the time of filing, the specification as originally filed did not support using Vezf1 to regulate expression of the endothelin-1 promoter.

Applicants provide the Stuhlmann declaration, which teaches Vezf1 would be useful for identifying endothelial cells and detecting arterial injury (3rd ¶). The declaration is not persuasive. Using Vezf1 to identify endothelial cells lacks specific utility because Xiong 1999 taught Vezf1 was specific to vascular endothelial cells and because the specification on pg 7, lines 11-13, only teaches identifying endothelial cells using Vezf1. The specification does not teach Vezf1 is specific to endothelial cells or

that Vezf1 is specific to vascular endothelial cells as described by Xiong 1999. The declaration teaches endothelial cells only express Vezf1 when proliferation is required which is not described in the specification. The specification concludes "Vezf1 expression is mainly confined to vascular endothelial cells and their precursors;" the specification does not conclude that Vezf1 expression is limited to proliferating vascular endothelial cells.

The asserted utilities in the specification have been addressed more specifically in the previous office action as follows:

Pg 7, 3rd full paragraph, states the invention provides for a method of identifying an endothelial cell by identifying expression of Vezf1 RNA or protein in the cell. However, applicants do not provide a reasonable correlation between Vezf1 expression and endothelial cells. The specification and the art at the time of filing do not teach that Vezf1 expression occurs only in endothelial cells; therefore, the asserted utility is not substantial. Pg 41, 1st full ¶, last sentence, states Vezf1 expression correlates to the beginning of blood island formation; it does not state Vezf1 expression in blood islands was limited to endothelial cells. Endocardial cells, which inherently comprise endothelial cells, did not express Vezf1 (¶ bridging pg 41-42, 2nd sentence; AP staining indicates Vezf1 expression as described in the preceding ¶). Strong expression was found in the allantois (pg 42, lines 5-6); however, the specification does not teach expression in the allantois was limited to endothelial cells. The specification concludes, "Vezf1 expression is mainly confined to vascular endothelial cells and their precursors." The term "mainly" in the statement implies more than just endothelial cells express

Vezf1 or that non-endothelial cells expressed Vezf1; therefore the asserted utility is not specific. The conclusion that vascular endothelial cells and their precursors express Vezf1 implies that the asserted utility would be generic to vascular endothelial cells and their precursors. Such a utility is not specific to one type of cell because endothelial cells and endothelial cell precursors have different structures and functions. At the time of filing applicants had merely begun to establish an expression pattern for Vezf1, which in and of itself is insufficient to establish a specific utility for using the Vezf1 gene as a marker for endothelial cells because Vezf1 gene expression is generic to vascular endothelial cells, their precursors and possibly other types of cells that have not been tested, and because Vezf1 expression did not occur in endothelial cells of the endocardium (¶ bridging pg 41-42).

Pg 7, 4th full paragraph, discusses using the Vezf1 gene to diagnose vascular disease. However, the specification and the art at the time of filing do not correlate Vezf1 expression with any vascular disease; therefore, the asserted utility is not specific to any vascular disease. In addition, the specification does not teach whether vascular disease correlates with overexpression or lack of expression of Vezf1; therefore, the asserted utility is not substantial. Finally, the specification does not describe any vascular diseases linked to overexpression of Vezf1 or a disruption in Vezf1; therefore, the asserted utility is not substantial.

Pg 7, 4th full paragraph, discusses using Vezf1 to treat vascular disease. However, the specification and the art at the time of filing do not correlate Vezf1 with any vascular disease; therefore, the asserted utility is not specific to any vascular

disease. In addition, the specification does not teach whether vascular disease correlates with an excess or an absence of Vezf1; therefore, the asserted utility is not substantial. Finally, the specification does not describe any vascular diseases linked to an excess or an absence of Vezf1; therefore, the asserted utility is not substantial.

Conclusion

No claim is allowed.

Inquiry concerning this communication or earlier communications from the examiner should be directed to Michael C. Wilson who can normally be reached at the office on Monday, Tuesday, Thursday and Friday from 9:30 am to 6:00 pm at 571-272-0738.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to (571) 272-0547.

Patent applicants with problems or questions regarding electronic images that can be viewed in the Patent Application Information Retrieval system (PAIR) can now contact the USPTO's Patent Electronic Business Center (Patent EBC) for assistance. Representatives are available to answer your questions daily from 6 am to midnight (EST). The toll free number is (866) 217-9197. When calling please have your application serial or patent number, the type of document you are having an image problem with, the number of pages and the specific nature of the problem. The Patent Electronic Business Center will notify applicants of the resolution of the problem within 5-7 business days. Applicants can also check PAIR to confirm that the problem has been corrected. The USPTO's Patent Electronic Business Center is a complete service center supporting all patent business on the Internet. The USPTO's PAIR system provides Internet-based access to patent application status and history information. It also enables applicants to view the scanned images of their own application file folder(s) as well as general patent information available to the public.

For all other customer support, please call the USPTO Call Center (UCC) at 800-786-9199.

If attempts to reach the examiner are unsuccessful, the examiner's supervisor, Amy Nelson, can be reached on 571-272-0804.

The official fax number for this Group is (703) 872-9306.

Michael C. Wilson

MICHAEL WILSON
PRIMARY EXAMINER